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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/078,808	02/19/2002	Manas Kumar Majumdar	08702.0086-00000	7146

7590 04/07/2004

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EXAMINER

ANDRES, JANET L

ART UNIT	PAPER NUMBER
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1646

DATE MAILED: 04/07/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

10/078,808

Applicant(s)

MAJUMDAR ET AL.

Examiner

Janet L. Andres

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE ____ MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 20 January 2004.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 11, 12, 21 and 23-31 is/are pending in the application.
- 4a) Of the above claim(s) ____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) ____ is/are allowed.
- 6) ☒ Claim(s) 11, 12, 21, 23-31 is/are rejected.
- 7) ☐ Claim(s) ____ is/are objected to.
- 8) ☐ Claim(s) ____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on ____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. ____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. ____. |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date ____. | 6) <input type="checkbox"/> Other: ____. |

RESPONSE TO AMENDMENT

1. Applicant's amendment filed 20 January 2004 is acknowledged. Claims 11, 12, 21, 23-29, and 31 are pending and under examination in this office action. The text of those sections of Title 35, U.S. Code, not included in this action can be found in a prior office action.

Claim Rejections/Objections Withdrawn

2. The objection to the specification is withdrawn in response to Applicant's amendment correcting the use of trademarks.

3. The rejection of claims 21, 23-29 and 31 under 35 U.S.C. 112, first paragraph, as lacking enablement commensurate in scope with the claims is withdrawn in response to Applicant's amendment limiting the methods to CD105+ non-expanded cells and a suitable matrix.

Claim Rejections Maintained

4. The rejection of claims 11 and 12 under 35 U.S.C. 102(a) and 102(e) as anticipated by the '328 patent and under 102(e) as anticipated by the '816 patent is maintained for reasons of record in the office action of 26 September 2003.

Applicant argues there is no indication in the prior art that BMPS affect IL-1-related damage in cartilage and there is no indication that IL-1 is involved. Applicant further argues that neither cited patent teaches the administration of the BMP to damaged cartilage and that IL-1 would be unlikely to be present in undamaged tissue. Applicant additionally argues that the claimed results do not necessarily flow from administering any amount of BMP.

Applicant's arguments have been fully considered but have not been found to be persuasive. As stated on p. 3 of the previous office action, administration of BMPs would inherently result in the effect on IL-1, regardless of whether that effect was appreciated at the

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time. Each patent does teach administration to damaged cartilage. In column 2, lines 54-60, the '328 patent teaches treatment of defects and of patients in need of cartilage formation. In column 7, lines 3-5, the '328 patent teaches treatment of cartilage damage. In the abstract of the '816 patent, treatment of cartilage defect by administration of BMP-9 is taught. Similar teachings are found in column 2, lines 20-26, and column 5, lines 14-17. In column 6, lines 19-21, the '816 patent teaches administration of BMP-9 to treat bone, cartilage, or tissue damage. Thus each patent teaches administration of BMPs under conditions in which IL-1 would, according to Applicant's teachings, be present, and the effect would have occurred regardless of whether it was recognized at the time. While the effect may not occur at all concentrations, Applicant's claims do not specify any ranges that would distinguish them from the prior art. There is nothing in Applicant's teachings to distinguish the amount effective for inhibition of IL-1 from the amount effective for cartilage repair. Thus Applicant's methods are not different from those taught by the prior art.

5. The rejection of claims 21 and 23-31 under 35 U.S.C. 102(a) as anticipated by WO 00/29552 is maintained for reasons of record in the office action of 26 September 2003.

Applicant argues that WO 00/29552 only teaches tissue culture expanded cells, whereas the claims are drawn to non-expanded cells. Applicant further argues that the claims require that the cells be a "specific population of CD105+ cells" and that this population is not taught by WO 00/29552.

Applicant's arguments have been fully considered but have not been found to be persuasive. As was stated in paragraph 6, p. 3, of the previous office action, WO 00/29552 teaches non-expanded cells on p. 10, lines 10-19. The cells are CD105 (endoglin) positive, as

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was stated in paragraph 6, p. 3, of the previous office action; expression of endoglin is an inherent and defining characteristic of the MSCs. See Barry et al., cited in the previous office action.

6. The rejection of claims 21 and 23-31 under 35 U.S.C. 103(a) as unpatentable over WO 00/29552 in view of the '819 patent is maintained for reasons of record in the office action of 26 September 2003.

Applicant argues that the instant MSCs are not the same as the MSCs taught by WO 00/29552 and that they are "not all" CD105+. Applicant further argues that, since WO 00/29552 is "insufficient for establishing a case of obviousness", the addition of information about BMP-9 will not render Applicant's invention any more obvious. Applicant further argues that the specification teaches unexpected advantages over the compositions of WO 00/29552, because adherence does not correlate with chondrogenic potential, whereas CD105/endoglin expression does, and because of the possibility that expansion alters cell surface characteristics.

Applicant's arguments have been fully considered but have not been found to be persuasive. It has not been stated that non-expanded cells are obvious over WO 00/29552; they are disclosed in WO 00/29552. See paragraph 5, above, and paragraph 6 of the previous office action. Applicant's specification teaches the use of cells purified using an anti-CD105 antibody but that is not what is claimed. Applicant's claimed methods do not require that the cells used be "all CD105+"; they require a composition comprising CD105+ cells, that is, a composition that contains CD105+ cells and can contain other cell types as well. No purification step resulting in "all CD105+" cells is required by the methods; all that is required is that a composition containing them be somehow isolated. MSCs are, as stated above and previously, CD105+.

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Thus the non-expanded cells taught by WO 00/29552 are also CD105+. Thus WO 00/29552 teaches methods using non-expanded compositions comprising CD105+ cells and those methods anticipate methods within the scope of Applicant's claims. Thus the claims were rejected under 35 U.S.C. 102(a) as anticipated by WO 00/29552. The '819 patent teaches a method that, combined in an obvious fashion - because they are drawn to the same purpose - with WO 00/29552, results in other methods within the scope of Applicant's claims. Thus the claims are also unpatentable over WO 00/29552 in view of the '819 patent.

7. The rejection of claims 11 and 12 under 35 U.S.C. 112, second paragraph, as indefinite in the recitation of "IL-1 activity" is maintained for reasons of record in the office action of 26 September 2003.

Applicant has amended the claims to specify that that the effect blocked is the effect on cartilage growth.

Applicant's amendment is insufficient to overcome this rejection because it does not specify what activity is intended. It appears from p. 27, example 6, that IL-1 inhibits the induction of several genes via downregulation of sox-9. The effects blocked by BMPs appear to be the decrease in Col2A1 and sox-9.

NO CLAIM IS ALLOWED.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire **THREE MONTHS** from the mailing date of this action. In the event a first reply is filed within **TWO**

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MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Janet L. Andres whose telephone number is 571-272-0867. The examiner can normally be reached on Monday-Thursday and every other Friday, 8:00-5:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Yvonne Eyler can be reached on 571-272-0871. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Janet L. Andres, Ph.D.
2 April 2004



JANET ANDRES
PATENT EXAMINER